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Archives of Medical Research ■ (2018) ■

Archives of Medical Research

REVIEW ARTICLE

Apolipoprotein E in Cardiovascular Diseases: Novel Aspects of an Old-fashioned Enigma

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Received for publication August 2, 2018; accepted August 24, 2018 (ARCMED_2018_254).

The presence of different APOE isoforms represents a well-known risk factor for cardiovascular diseases. Besides the pleiotropic effects of APOE polymorphism on heart and neurological diseases, this review summarizes the less-known functions of APOE and the possible implications for cardiovascular disorders. Beyond the role as lipid transporting protein, its involvement in lipid membrane homeostasis and signaling, as well as its nuclear transcriptional effects suggests a more complex role of APOE, receiving great interest from researchers and physicians from all medical fields. Due to the presence of different APOE isoforms in human population, understanding APOE's role in pathological processes represents not only a challenge, but a demand for further development of therapeutic strategies for cardiovascular diseases.

Key Words: ApoE polymorphism, Lipids, Cell membrane, Cardiovascular diseases.

Introduction

Apolipoprotein E (APOE) is a ubiquitous protein, essential for the lipid metabolism in all tissues and organs. Because of the numerous evidences about APOE involvement in a wide range of chronic conditions, it is believed that its role is widely known and accepted. Nevertheless, the multifunctional role of APOE beyond its involvement in lipid metabolisms, made it become a real biologic enigma. In this review, we summarize well-known effects of APOE, as well as their lipid-independent effects in different pathological conditions, trying to speculate the dimension of the consequences on cardiovascular diseases.

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The Well-known Face of Apolipoprotein E

APOE is a protein member of soluble apolipoproteins, coded by three alleles (ε2, ε3, ε4) (1). Thus, these alleles give six phenotypes (from most to least common subsequently: ε3/ε3, ε4/ε3, ε3/ε2, ε4/ε4, ε4/ε2, and ε2/ε2) (2). Although APOE is synthesized mainly by liver (3), many other cells and tissues are able to synthesized APOE, such as macrophages, adipocytes, smooth muscle cells, brain or kidney (4,5). One of the major functions of APOE is to maintain cholesterol homeostasis and lipoprotein clearance from circulation. Lipids absorbed from the intestine are transported to different tissues by chylomicrons particles via lymphatic system. After restoring tissue energetic reserves and/or adipocyte lipid storage, chylomicrons acquire APOE, which acts as a ligand for cell-surface receptors of low-density lipoprotein receptor (LDLR) family. Thus, the liver cells possessing low density lipoprotein

0188-4409/$ - see front matter.
https://doi.org/10.1016/j.arcmed.2018.08.008